REMARKS

Claims 1-29 were cancelled and new claims 30-39 were added in the Preliminary Amendment filed October 23, 2003. Claims 30-39 are pending. Applicants hereby reserve the right to pursue the subject matter of the canceled claims in one or more divisional patent applications.

Claim Rejections Under 35 U.S.C. § 101

Claims 37-39 are rejected under 35 U.S.C. § 101, as being directed to non-statutory subject matter.

Applicants respectfully traverse.

The Examiner asserts that claims 37-39 read on cells naturally present in the tissue of an animal subject, including animal CNS and brain tissue. The Examiner further asserts that in claims 37-39, a purified pluripotent brain stem cell may be returned to the *in vivo* environment from which it was originally derived in unaltered form.

Claims 37-39 depend on claim 30 which states that the stem cell is "purified" i.e. by the hand of man. Therefore, claims 37-39 depend on subject matter which has been isolated and purified. Applicants describe in detail in the Examples section how these cells were purified and cultured. The Examiner's assertions that these cells are "exactly" the same i.e. unaltered form is incorrect. In order to expedite prosecution Applicants have amended the claims to indicate that the stem cells were "isolated."

In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

Claim Rejections Under 35 U.S.C. § 112, Written Description

Claims 33 and 35 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

Applicants respectfully traverse.

The Examiner asserts that claim 33 and 35 encompass any mammalian pluripotent stem cell; any murine pluripotent stem cell.

Applicants have described the stem cells and identified the actual markers that identify these stem cells, i.e. Type I, II and II cells. Applicants also provide detailed morphological and phenotypic descriptions. The Examiner asserts that the specification does not provide additional species for these types of cells. However, the identified markers that categorize these cells are the hallmarks of these cells and can be identified in any species that bears the counterpart marker of these cells. Also, the morphological and phenotypic data can be combined with these markers to identify these cells in different mammals. For example, page 5, lines 11-31 describe the phenotypic and morphological data:

> Figure 1 shows phase contrast and electron microscopic images of type I, II, and III clones. Figures 1A, 1C, and IE are phase contrast images of type I, II and III clones of cultured adult brain cells, respectively. Figures 1B, 1D, and IF show type I, II and III spheres counterstained with propidium iodide, respectively. Scale bars for Figures 1A-F are 40, 30, 20, 30, 20, and 30 microns, respectively;
>
> Figure 2 depicts the types of spheres found in the culture paradigm of the invention, and the generation conditions for the appearance and evolution of sphere types from brain;
>
> Figure 3 shows the phase and electron microscopic images of type II (A and B) and type III (C and D) spheres. Scale bars for Figures 3A-D are 10, 5, 15, and 2 microns, respectively;
>
> Figure 4 shows immunostaining of early and late type II and type III spheres. Scale bars for Figures 4A, G and J are 10 microns, Figures 4B and 4C are 15 microns, Figures 4E and 4F are 30 microns, Figure 4H is 20 microns, and Figure 4I is 100 microns;
>
> Figure 5 shows the evolution and proliferation of type II (Figure 5A and SC), and type III (Figures 5B and SD) spheres. Scale bars for

Figures 5A and SB are 25 microns, and for Figures 5C and 5D are 10 microns;

Figure 6 shows type II and type III spheres from ROSA-26 transgenic mice. Scale bars for Figure 6A is 50 microns, and Figure 6B is 30 microns; and

Figure 7 shows phase and electron microscopy of a type II adult mouse and type II adult human sphere. The adult mouse sphere is approximately 100 microns in diameter, while the adult human sphere is approximately 200 microns in diameter.

Applicants describe the isolation of these cells, see, for example page 6, lines 5-23:

Cell separation and cell adhesion can be manipulated using a variety of contact-limiting and contact-inhibiting factors. For example, chemical-separating agents such as mercaptoethanol, physical separating agents such as methylcellulose, and anti-adhesives such as poly 2-hydroxyethyl methacrylate are used to deter cell-cell and cell-substrate associates during the initial isolation of stem/precursor cells from the newly-dissociated brain. This allows the "purification" of these cells from mature, differentiated neurons and glia that are also dissociated during the brain dissociation procedures. The mature, differentiated neurons and glia cannot survive these anti-adhesion, anti-cell interaction procedures. Thus, agents such as mercaptoethanol are always used in the first stage of isolation of type I and II clones to help deter the survival of the more mature cellular elements (by deterring their clustering). At the same time, agents such as mercaptoethanol may have certain growth-promoting actions on the single stem/precursor cells that eventually proliferate to form these early sphere types.

Since cell-cell and cell-substrate interactions are important for cellular differentiation, contact-inhibiting (or contact-limiting) factors as mercaptoethanol are eventually removed from the culture medium for the evolution or differentiation of type II and type III spheres.

The differentiation of type m spheres requires other additional factors, including growth factors like beta fibroblast growth factor, epidermal growth factor, or such factors that are also contained within pituitary extract. Such additional factors are described in the type III culture media discussed below (see, Example 3).

Further Applicants describe the types of purified stem cells. See, for example, page 7, lines 16-33 through to page 12, lines 1-6. Applicants provide more than enough detail wherein one of ordinary skill in the art can identify and purify these stem cells.

In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

Claim Rejections Under 35 U.S.C. § 112, Scope of Enablement

Claims 30-39 are rejected under 35 U.S.C. § 112, first paragraph.

Applicants respectfully traverse. However, in order to compact and expedite prosecution Applicants have amended the claims as per the Examiner's recommendations. These amendments were made solely for purposes of expediting prosecution and are not meant to be construed as surrender of any subject matter. Applicants reserve the right to further prosecute the subject matter in one or more Divisional or Continuation applications.

In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

Claim Rejections Under 35 U.S.C. § 102

Claims 30-33, 35 and 37-38 are rejected under 35 U.S.C. § 102(b) by Boss *et al.*

Claims 30-39 are rejected under 35 U.S.C. § 102(e) by Johe *et al.*

Claims 30-33 are rejected under 35 U.S.C. § 102(e) by Weiss *et al.*

Applicants respectfully traverse. None of these references teach the markers that identify each of these isolated stem cells, the methods of isolating them or differentiate them into Type I, II or III type clones. However, in order to expedite prosecution Applicants have amended the claims. These amendments are deemed to overcome the Examiner's rejections. In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant invention.

CONCLUSION

Applicants have made every effort to present claims which distinguish over the cited art, and it is believed that all claims are now in condition for allowance. However, Applicants request that the Examiner call the undersigned (direct line 561-671-3666) if anything further is required by the Examiner prior to issuance of a Notice of Allowance for all claims.

Applicants respectfully request entry of the foregoing amendments and remarks and reconsideration and withdrawal of all rejections. It is respectfully submitted that this application with claims 30-39 is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with the Applicants' attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at telephone number shown below.

Although, Applicants believe that no extensions of time are required with submission of this paper, Applicants request that this submission also be considered as a petition for any extension of time if necessary. The Commissioner for Patents and Trademarks is hereby authorized to charge the amount due for any retroactive extensions of time and any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees paid on the filing or during prosecution of this application to Deposit Account No. 50-0951.

Respectfully submitted,

AKERMAN SENTERFITT

Date: January 30, 2006

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Docket No. 7230-8